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nucleotide sequence encoding the N-terminus of the zP450RAI cDNA to identify fragments of the genomic clones which encode the N-terminal region. A 772 base pair PstI fragment which hybridized with the oligonucleotide probe was purified, ligated into the vector SK+ and sequenced using the Core Facility for Protein/DNA Chemistry at Queen's University, Kingston, Canada. Sequence analysis identified this clone as containing the putative initial methionine followed by 129 base pairs of coding sequence, plus 651 nucleotides upstream (5'). Within this 772 base pair fragment, a 402 base pair HindIII fragment was found to contain the putative retinoic acid response element (RARE). This fragment was subcloned into the pGL3B luciferase vector, in both the forward and reverse orientations, (Promega) for transient transfection analyses.

In accordance with 37 C.F.R. §1.121(b)(iii), we enclose separate pages headed "SPECIFICATION - Version showing changes made" in which all the changes to the specification made relative to the previous version are shown explicitly, inserted passages being indicated by underlined boldface type, deleted passages being in boldface type enclosed in square brackets.

IN THE CLAIMS

In accordance with 37 C.F.R. §1.121(c), please amend the claims by amending the claims submitted on or about February 20, 2001 to read as follows:

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83. (Once amended) An isolated protein which oxidizes a retinoid and encoded by a nucleic acid molecule comprising a nucleotide sequence that hybridizes under high stringency conditions, wherein high stringency conditions include a wash step of about 0.2x SSC at 50°C, to a polynucleotide having a nucleotide sequence selected from the group of sequences shown as: SEQ ID NO:3; a sequence which varies from SEQ ID NO:3 in a coding region due to the degeneracy of the genetic code; SEQ ID NO:5; a sequence which varies from SEQ ID NO:5 in a coding region due to the degeneracy of the genetic code; SEQ ID NO:31; a sequence which varies from SEQ ID NO:31 in a coding region due to the degeneracy of the genetic code, or a conservatively substituted amino acid variant of a said protein which oxidizes a retinoid.



- 84. (Once am nded) The isolated protein of claim 83 in which the nucleic acid molecule comprises a nucleotide sequence selected from the group of sequences identified as SEQ ID NO:3, a sequence which varies from SEQ ID NO:3 in a coding region due to the degeneracy of the genetic code, SEQ ID NO:5, a sequence which varies from SEQ ID NO:5 in a coding region due to the degeneracy of the genetic code, SEQ ID NO:31, and a sequence which varies from SEQ ID NO:31 in a coding region due to the degeneracy of the genetic code.
- 65. (Once amended) The isolated protein of claim 83 in which the sequence of the nucleic acid molecule comprises a part of a human, fish or mouse genome.
- 89. (Once amended) The isolated protein of claim 83 in which the nucleic acid molecule encodes a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:4, SEQ ID NO:32, and conservatively substituted amino acid variants of SEQ ID NO:2, SEQ ID NO:4, and SEQ ID NO:32 which oxidizes a retinoid.
- 90. (Once amended) An isolated protein which hydroxylates a retinoid at the 4-position of the ß-ionone ring and encoded by a nucleic acid molecule comprising a nucleotide sequence that hybridizes under high stringency conditions, wherein high stringency conditions include a wash step of about 0.2x SSC at 50°C, to a nucleic acid molecule having a nucleotide sequence selected from the group of sequences shown as: SEQ ID NO:3; a sequence which varies from SEQ ID NO:3 in a coding region due to the degeneracy of the genetic code; SEQ ID NO:5; a sequence which varies from SEQ ID NO:31; a sequence which varies from SEQ ID NO:31 in a coding region due to the degeneracy of the genetic code; or a conservatively substituted amino acid variant of a said protein which hydroxylates a retinoid.
- 91. (Once amended) The isolated protein of claim 90 in which the nucleic acid molecule comprises a nucleotide sequence selected from the group of sequences identified as SEQ ID NO/3, SEQ ID NO:5, and SEQ ID NO:31.
- 92. (Once amended) the isolated protein of claim 90 in which the sequence of the nucleic acid molecule comprises a part of a human, fish or mouse genome.



95. (Once amended) The isolated protein of claim 90 in which the nucleic acid molecule encodes a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, and SEQ ID NO:32, or a conservatively substituted amino acid variant of a said protein which hydroxylates a retinoid.

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97. (Once amended) An isolated polypeptide which binds to an antibody elicited by a protein having the amino acid sequence SEQ ID NO:2 wherein the antibody is elicited by an epitope located within an unconserved region of the protein, the unconserved region consisting of amino acids 1 to 432 of SEQ ID NO:2.

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99. (Once amended) An isolated polypeptide which binds to an antibody elicited by a protein having the amino axid sequence SEQ ID NO:4 wherein the antibody is elicited by an epitope located within an unconserved region of the protein, the unconserved region consisting of amino acids 1 to 436 of SEQ ID NO:4.

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- 101. (Once amended) An isolated polypeptide which binds to an antibody elicited by a protein having the amino acid sequence SEQ ID NO:32 wherein the antibody is elicited by an epitope located within an unconserved region of the protein, the unconserved region consisting of amino acids 1 to 436 of SEQ ID NO:32.
- 104. (Once amended) The polypeptide of claim 97 encoded by a nucleic acid molecule comprising a nucleotide sequence that hybridizes under high stringency conditions, wherein high stringency conditions include a wash step of about 0.2x SSC at 50°C, to the nucleotide sequence shown as SEQ ID NO:3.

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- 105. (Once amended) The polypeptide of claim 99 encoded by a nucleic acid molecule comprising a nucleotide sequence that hybridizes under high stringency conditions, wherein high stringency conditions include a wash step of about 0.2x SSC at 50°C, to the nucleotide sequence shown as SEQ ID NO:5.
- 106. (Once amended) The polypeptide of claim 101 encoded by a nucleic acid molecule comprising a nucleotide sequence that hybridizes under high stringency conditions, wherein high stringency conditions include a wash st p of about 0.2x SSC at 50°C, to the nucleotide sequence shown as SEQ ID NO:31.